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ISOLATION AND STRUCTURAL ELUCIDATION OF TWO NEW ALKALOIDS FROM PAPAVER MACROSTOMUM BOISS. ET HUET

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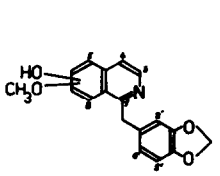
The plant Papaver macrostomum Boiss. et Huet was found to contain two new alkaloids which were named sevanine and macrostomine. Sevanine, obtained from the phenolic fraction, m.p. 218°, showed M^+ at mass 309,0989 corresponding to $C_{18}H_{15}NO_4$ (309.1001), M-1 (b.p.) and a weak peak at m/e 135 (methylenedioxy benzylic ion). The UV spectrum exhibited λ_{max}^{EtOH} nm (log ε) 241 (4.74), 277^{sh} (3.82), 285 (3.87), 291^{sh}(3.85), 321 (3.69), and 332 (3.73); it was practically identical with the UV spectra of papaverines[1]. Addition of sodium hydroxide caused a bathochromic shift of the long wavelength band to 362 nm which is characteristic for the hydroxysubstituted aromatic chromophore. The PMR spectrum ($CDCl_3$) (ref. 2) of sevanine showed singlets at 3.88 ppm (3H) for a methoxyl group, 4.45 (2H) for benzylic protons, and 5.87 (2H) for a methylenedioxy group. The pair of doublets at 7.45 (H-4) and 8.23 (H-3) (J=6.0), the three proton singlet at 6.72 (H-2',5',6'), and the two one-proton singlets at 7.10 and 7.48 (H-5,8) are assignable to aromatic protons. Thus, sevanine is 1-(3',4'-methylenedioxybenzyl)-6,7-hydroxymethoxyisoquinoline (I).

Chromatography on alumina of the nonquaternary fraction gave macrostomine, m.p. 107-110° (benzene), $[\alpha]_D^{25}$ -51° ± 3° (c 0.892 in $CHCl_3$), methiodide,



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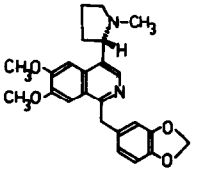

II

m.p. 220-230° (methanol). Mass spectrum: M^+ 406.1892 ($C_{24}H_{26}N_2O_4$, th. 406.1892), m/e 84 (b.p. $C_5H_{10}N$, N-methylpyrrolidinium[3]), 135 ($C_8H_7O_2$, methylenedioxy benzylic ion), and 271 ($M-C_8H_7O_2$). The UV spectrum exhibited λ_{max}^{EtOH} nm (logε) 241 (4.87), 246^{sh}(4.62), 276^{sh}(3.87), 288 (3.97), 292^{sh}(3.80), 317 (3.74), and 332 (3.77); it is similar to those of sevanine (I) and of other papaverine alkaloids. $\lambda_{Max}^{Ethanolic\ HCl}$ nm (logε) 259 (4.63), 290 (3.74), 319 (3.84), and 333^{sh}(3.73). The IR spectrum indicated the presence of the methyl group attached to nitrogen in an aliphatic amine (band at 2793 cm^{-1}), and aromatic rings. The PMR spectrum (C_6D_6) exhibited a three proton singlet at 2.13 ppm assigned to the N-CH_3 group, multiplets in the range 1.5-2.2 (4H) and 3.0-3.6 (3H) assigned to protons of the pyrrolidine moiety. The signals at 3.47, 3.55, and 5.30 are attributable to two methoxyls and one methylenedioxy group. The singlet at 4.55 (2H) is assignable to benzylic protons. The other signals, 6.97d (J=1.0) (H-2′), 6.55d (J=8.0) (H-5′), 6.80q (J=1.0; 8.0) (H-6′), 7.35s (H-8), 7.87s (H-5), and 8.72s (H-3) are attributable to aromatic protons. The PMR spectrum of macrostomine in trifluoroacetic acid shows the N-methyl signal as a doublet at 3.08 (J=5.0) which is converted to a sharp singlet in CF_3COOD. From that follows the assignment of structure II to macrostomine.

Similarly to the longest wavelength Cotton effect of (S)-(-)-nicotine[4] or (S)-(-)-brevicolline[5] that of macrostomine (II) (ref. 6) is negative. On the basis of this fact it is assumed that the configuration of macrostomine may also be S.

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2. PMR spectra were measured with TMS as internal standard at 60 MHz. Coupling constants are quoted in Hz.
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6. CD data (in ethanol) of macrostomine (II): 331 nm (-0.46), 317 (-0.39), 298 (-0.44), and 273 (+0.33); (S)-(-)-nicotine: 270 nm (-0.19), 263 (-0.18), 258^{sh} (-0.08), and 244 (+0.08).